DEPARTMENT OF DEFENSE
ARMED SERVICES BLOOD PROGRAM OFFICE
5109 LEESBURG PIKE
FALLS CHURCH, VA 22041-3258

REPLY TO
ATTENTION OF

ASBPO (40-2b)

BPL 02-02
18 November 2002

MEMORANDUM FOR SEE DISTRIBUTION

SUBJECT: Nucleic Acid Testing (NAT) for the Human Immunodeficiency Virus (HIV-1 and the Hepatitis C Virus (HCV) in Blood Donors

1. The Armed Services Blood Program Office (ASBPO) was established by the Assistant Secretary of Defense for Health Affairs (ASD(HA)) to coordinate the blood programs of the Military Services and the Unified Commands. In that respect, the ASBPO is issuing Blood Program Letter (BPL) 02-02 notifying the Services of the policy regarding Nucleic Acid Testing (NAT) for the Human Immunodeficiency Virus (HIV-1) and the Hepatitis C Virus (HCV) in blood donors.

2. The ASD (HA) issued a memorandum, Nucleic Acid Testing (NAT) for the Human Immunodeficiency Virus (HIV-1) and the Hepatitis C Virus (HCV) in Blood Donors, to the Services Secretaries on 13 May 1999. The memorandum required each Service to implement HIV-1 and HCV NAT under an investigational new drug (IND) protocol on all blood donations. The Food and Drug Administration (FDA) announced on 28 February 2002 that the first HIV-1 and HCV NAT test kit had been licensed for use in screening blood donors, (Encl 1). Therefore, the Services will implement FDA licensed single-donor NAT for HIV-1 and HCV as soon as possible, but no later than 30 January 2003. With the implementation of FDA licensed NAT for HIV-1/HCV, all blood and blood components collected by the Department of Defense will no longer be tested for HIV-1 Antigen.

3. Services must establish local contingency contracts for alternate nucleic acid testing sites to ensure the continuous availability of licensed blood products for military operations and national emergencies. Alternate nucleic acid testing sites should utilize licensed single-donor NAT, but mini-pool NAT technology is an acceptable alternative if single-donor NAT is not available.

4. Following implementation of the FDA licensed NAT for HIV-1/HCV, existing Investigational New Drug (IND) protocols for NAT will no longer be utilized and obtaining informed consent from blood donors prior to blood collection will no longer be required. The IND protocol must be kept open with their Institutional Review Board (IRB) if a collection facility under that IRB has any donors enrolled under the follow-up protocol. The IND protocols may be closed with their respective IRB only when all cases have been completed and closed. All records pertaining to the NAT IND for HIV-1/HCV must be retained for a minimum of two years from the implementation date of the licensed test.

5. Blood Donor Centers will comply with the enclosed *Nucleic Acid Testing Algorithm* and *NAT Product, Donor, and Recipient Management Table* (Encls 2 and 3); however, these enclosures are subject to change when the FDA publishes final guidance documents.

6. If NAT results are reactive, all blood and blood components prepared from the donation will be quarantined for destruction and shall not be used for transfusion or for the manufacture of any product. Except during emergencies, blood products will not be released

for transfusion unless they are non-reactive for HIV-1 and HCV by NAT. If blood products must be released for transfusion before NAT can be performed, emergency release protocols will be utilized in accordance with Service Standard Operating Procedures (SOPs) and the current version of the Armed Services Blood Program Guidelines for Infectious Disease Screening and Lookback of Blood Donations. However, red blood cells, which are intended for freezing, may be shipped to the Armed Services Whole Blood Processing Laboratories prior to the completion of NAT with the approval of the Service Blood Program Officer and the Director, Armed Services Blood Program Office.

7. The DBSS testing profile and donor deferral codes specific for NAT are being developed and are not available in DBSS v3.04. However, if NAT result(s) are reactive, all blood and blood components prepared from the donation must still be appropriately quarantined and destroyed in DBSS and donors must be appropriately deferred. Until specific NAT testing profiles and donor deferral codes are available, Nucleic Acid Test multiplex (HIV-1/HCV) results must be entered in the Defense Blood Standard System (DBSS) under a designated test for NAT. This test must be set as mandatory in DBSS to ensure that blood components are appropriately quarantined and not released without NAT negative results.

a. Reactive HIV-1 NAT: Use DBSS deferral code 524 (HIV RR Confirmed Positive) to enter HIV-1 NAT reactive discriminatory assay results if the EIA is also repeat reactive. If the EIA is negative, use the permanent deferral code 908. A comment must be entered with the deferral code to designate that the results were obtained from HIV-1 RNA NAT.

b. Reactive HCV NAT: Use DBSS deferral code 515 (RR HCV) to enter HCV NAT reactive discriminatory assay results if the EIA is also repeat reactive. If the EIA is negative, use the permanent deferral code 908. A comment must be entered with the deferral code to designate that the results were obtained from HCV RNA NAT.

c. Equivocal HIV-1/HCV NAT: If seropositive for HIV or HCV, follow current donor deferral guidelines for HIV-1/2 or HCV. If seronegative, use DBSS indefinite deferral code 906 until the Alternate NAT is completed and the donor status can be resolved. A comment must be entered with the deferral code to designate that the results were obtained from HIV-1/ HCV RNA NAT.

8. Labeling changes must be made to both the Circular of Information (COI), dated August 2000, and to recovered plasma labels. Use of the COI dated Jul 2002 requires no additional label change. Plasma brokers should provide labels for the recovered plasma that reflect testing status for licensed HIV-1 RNA and HCV RNA. Labels for the COI (and recovered plasma if needed) should be printed and affixed to the COI and/or the recovered plasma units. The wording for labeling is subject to change whenever the FDA publishes final guidance documents. In the interim, the following wording must be used as written with no variances:

a. For COI Labels: "Licensed nucleic acid tests (NAT) for HCV RNA and HIV-1 RNA have been performed and found to be non-reactive. HIV-1 Ag testing is no longer required when using a licensed test for HIV-1 RNA, and therefore HIV-1 Ag testing was not performed. Date Implemented_____"

b. For Recovered Plasma Labels: "Recovered Plasma Label – Negative by tests for antibodies to HIV, HCV, HTLV I/II, HBc, and non-reactive for HBsAg, STS, HCV RNA, and HIV-1 RNA"

9. **Service Blood Program Officers and Combatant Command Joint Blood Program Officers** must complete the enclosed form, *Acknowledgment of Receipt and Implementation*, (Encl 4) and return the signed original or fax copy to the ASBPO **NLT 30 January 2003.** A copy of all Service policy documents/letters implementing this BPL must also be forwarded within 30 days of implementation. The ASBPO point of contact for this action is Commander B. G. Bartley. She can be reached at DSN 761-1736/8024, commercial (703) 681-1736/8024, or via e-mail at brenda.bartley@otsg.amedd.army.mil.

G. MICHAEL FITZPATRICK
COL, MS, USA
Director

Encls

DISTRIBUTION:
HQDA (DASG-ZA)
CNO N931
HQ USAF/SG

CF:
ODASD (FHP&R)
ODASD (C&PP)
JS, J4-MRD
HQ USJFCOM/JO2M
HQ USEUCOM/ECMD
HQUSPACOM/J07
HQ USSOUTHCOM/SCSG
HQ USCENTCOM/CCSG
DIR USPACOM JBPO
SBPO USAF
SBPO USA
SBPO USN

AF Lab Consultant
Army Lab Consultant
Navy Lab Consultant

FDA Talk Paper

FDA Talk Papers are prepared by the Press Office to guide FDA personnel in responding with consistency and accuracy to questions from the public on subjects of current interest. Talk Papers are subject to change as more information becomes available.

T02-13
February 28, 2002

Media Inquiries: 301-827-6242
Consumer Inquiries: 888-INFO-FDA

FDA APPROVES FIRST NUCLEIC ACID TEST (NAT) SYSTEM TO SCREEN WHOLE BLOOD DONORS FOR INFECTIONS WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV) AND HEPATITIS C VIRUS (HCV)

The Food and Drug Administration has licensed the first nucleic acid test (NAT) system intended for screening donors of whole blood and blood components intended for use in transfusion. This test system can simultaneously detect the presence of HIV and HCV in blood using a semi-automated system and is expected to further ensure the safety of whole blood and blood components, including fresh plasma, red cells and platelets, by permitting earlier detection of HIV and HCV infections in donors.

FDA also recently licensed the first NAT system for screening donors of plasma for the specific use in products that will be further manufactured, such as clotting factors and immune globulins.

The approved test system was developed by Gen-Probe Inc., San Diego, Calif. and will be distributed by Chiron Corporation, Emeryville, Calif.

Blood donors have been tested for evidence of HIV infection since 1985 and for evidence of HCV infection since 1990. Although increasingly sensitive tests for detection of HIV and HCV antibodies and HIV antigen were implemented during the past decade, in rare instances infections in donors have been missed.

The NAT system is capable of detecting more infectious donations than current tests because it detects viral genes rather than antibodies or antigens (proteins from the virus). Detection of viral genes permits detection earlier in the infection since the appearance of antibodies requires time for the donor to develop an immune response, and since detection of antigens requires time for a higher level of virus to appear in the bloodstream.

This new technology detects very small amounts of genetic material by copying the genes numerous times, resulting in a billion-fold amplification of the target gene. The approved test system can detect ribonucleic acid (RNA) from HIV-1 and HCV when tested in pools of 16 samples obtained from multiple donors. In a less automated format, it can also be used to test individual samples from whole blood collections. If a test pool is positive for either virus, the individual donation suspected of containing a virus can be identified and not transfused. The donor can be deferred from donating blood and notified.

Currently, donors of blood and plasma are tested for antibodies to HCV, antibodies to HIV and HIV-1 antigens, which are the virus's own proteins. However, there is still a "window period" during which a donor can be infected, but have negative screening tests. With the use of NAT for HCV, the window period is reduced by approximately 57 days (from an average of 82 days to 25 days). For HIV-1, the average window period with antibody is 22 days. This window period is reduced approximately to 16 days with antigen testing and to 12 days with NAT.

In nation-wide clinical trials performed to support the approval of the test on pools, a total of 7 HIV-1 positive and 88 HCV positive donations were detected in more than 20 million donations tested confirming the effectiveness of the test. The NAT system using pools was evaluated at eight volunteer blood donor sites while NAT for use with individual donations used data from U.S. military blood donor sites.

The use of the licensed test will allow blood banks that implement it to discontinue antigen testing, although blood donations will continue to be tested by antibody tests. FDA plans to issue guidance on the use of NAT in the near future.

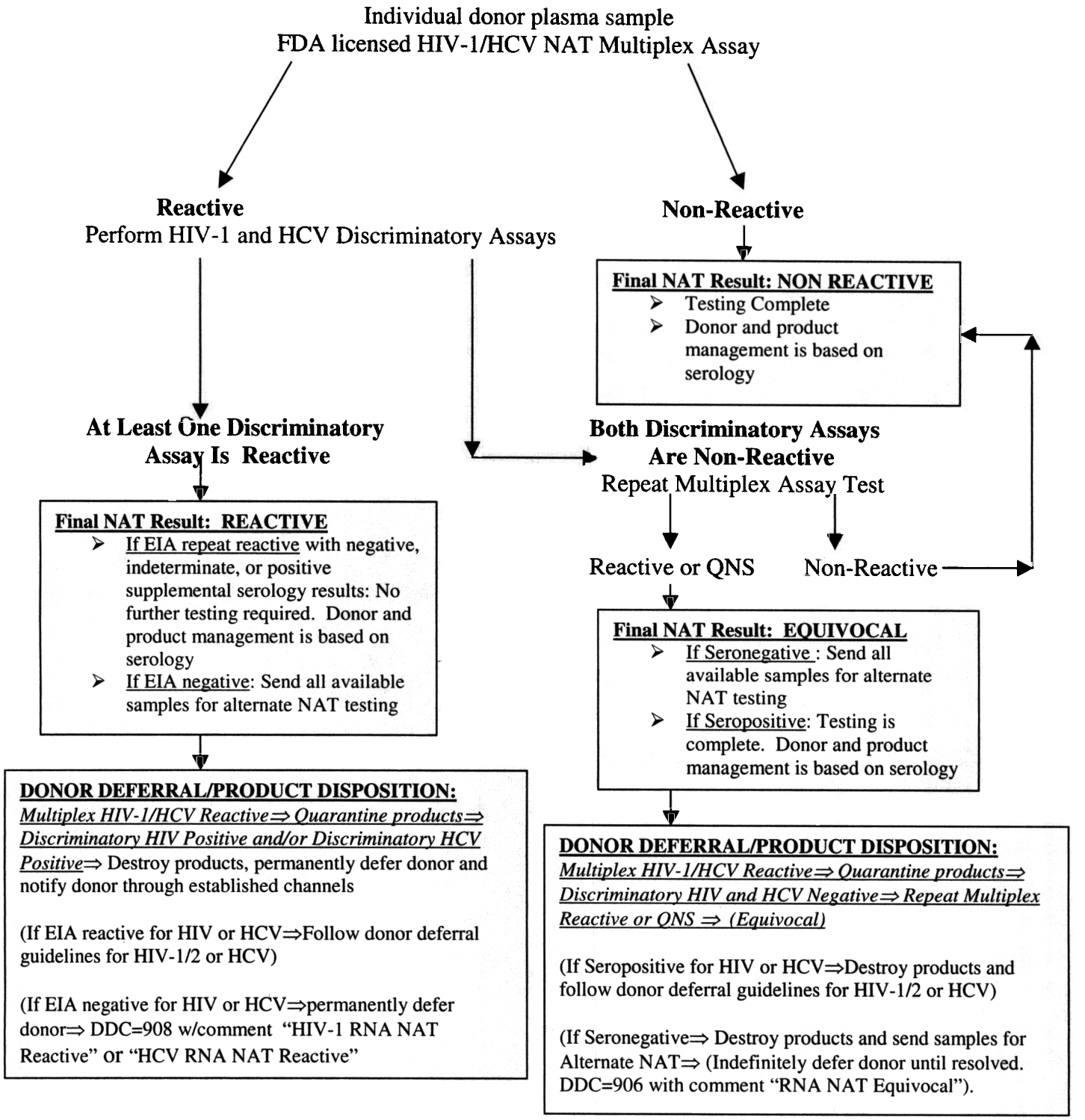
Since 1997, FDA has encouraged the large-scale study of NAT through the use of experimental protocols. More than one test system is under development. Most of the nation's blood establishments now participate in these experimental protocols. The Gen-Probe NAT system is the first to be approved to screen donors of whole blood and blood components intended for use in transfusion.

###

FDA News Page **FDA Home Page**

Office of Public Affairs
Web page uploaded by tg 2002-FEB-28.

NUCLEIC ACID TESTING ALGORITHM



DDC= Donor Deferral Code
MMCA= Military Medical Command Authority

NAT Product, Donor, and Recipient Management Table

Result	Current Product	Prior Donation Quarantine	Quarantine and Notify Consignee of Prior Donations	Donor Deferral and Notification	Recipient Notification
HIV-1 NAT Reactive	Quarantine	5 Years or 12 months prior to latest Negative NAT	Within 72 hours	Notify donor through established channels	Recipient of blood products collected within 5 years or 12 months prior to latest negative licensed screening test
HCV NAT Reactive	Quarantine	Indefinitely to extent that records exist or 12 months prior to the latest Negative NAT	Within 72 hours	Notify donor through established channels	Recipient of blood products collected within 10 years or 12 months prior to latest negative licensed screening test
Equivocal (Reactive in the Multiplex Assay, Non-Reactive in both Discriminatory Assays, with QNS or Reactive in repeat Multiplex Test)	Quarantine	If Alternate NAT is reactive, follow HIV-1 and HCV Reactive NAT guidelines above. If Alternate NAT is non-reactive, no action required.	Within 72 hours	If seropositive, follow HIV-1 and HCV donor deferral guidelines. If seronegative, indefinitely defer (Code 906) until resolved.	If Alternate NAT is reactive, follow recipient notification guidelines for HIV-1 NAT and HCV NAT If. If Alternate NAT is non-reactive, no action required.

ARMED SERVICES BLOOD PROGRAM OFFICE
5109 LEESBURG PIKE
FALLS CHURCH VA 22041-3248
703-681-8024/8025

ACKNOWLEDGMENT OF RECEIPT AND IMPLEMENTATION

Service Blood Program Officers and Combatant Command JBPOs only: Complete this Acknowledgment of Receipt and Implementation and retain one copy in your file. Return the signed original or fax copy to the Armed Services Blood Program Office **NLT 30 January 2003.**

BPL 02-02

Nucleic Acid Testing (NAT) for the Human Immunodeficiency Virus (HIV-1) and the Hepatitis C Virus (HCV) in Blood Donors

18 November 2002

The document listed above was received and the policy implemented by:

SERVICE/COMBATANT COMMAND:_____

DATE RECEIVED:_____

DATE IMPLEMENTED/OR:_____
PROJECTED IMPLEMENTATION

SIGNATURE:_____

NAME/TITLE:_____

For ASBPO use only

Date Returned:_____